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MS Italian patients manifesting natalizumab-related PML between 2009 and 2014. Report of the Italian group for MS-PML study

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Objective: To describe the progressive multifocal leukoencephalopathy (PML) and immune reconstitution inflammatory syndrome (IRIS) course, treatment and outcomes and to describe the features of epileptic seizures.

Design and methods: clinical and neuroradiological data of 34 MS patients who manifested natalizumab-related PML from November 2009 to December 2014 were obtained from 25 Italian Multiple Sclerosis (MS) Centres and analyzed in the current work.

Results: 29/34 patients survived to PML. 3 patients died within 6 months from the PML insurgence due to JC virus (JCV) brain infection and 2 patients died within 3 years due to long term bed immobility. PML disability peak was observed at the 6th month (mean EDSS increases of 1.2 points compared to the time of PML insurgence) and, at one year follow up, the mean EDSS still was 0.7 points higher compared to the time of insurgence. 29 patients were positive to JCV antibodies (the data is not available yet for 5 patients); higher number of CSF virus copies was related to the worse clinical course or death. Lower MRI lesion widening and monofocal presentation were related to a better clinical evolution, except for the subtentorial lesion locations.

19/34 patients manifested IRIS and a subacute clinical worsening in the first 5 months after PML onset; 15 out of the above 19 patients were treated with intravenous steroids with clinical improvement.

Epileptic seizures were observed in 10/34 patients (29.5%), 2 of them at PML onset, 5 during IRIS and 3 after PML recovery. 2 patients were presenting with generalized tonic-clonic seizures, 1 with status epilepticus and 7 with focal attacks. Drugs showed poor efficacy during the acute phase of epilepsy, however their efficacy improved over time.

Conclusions: Most of patients survived to PML but manifested a slightly long term worsening of their clinical condition. Steroid treatment of IRIS might reverse the IRIS-related disability increment. Epileptic seizures were commonly observed in PML and a progressive improvement of pharmacological response can be expected during the follow-up.

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